Remarks

The Office Action mailed September 15, 2004 has been received and reviewed. Claims 1-4, 11, 12, 14, 16, 18, 22, 109, and 110 having been amended, the pending claims are claims 1-24, 48, 100-110. Reconsideration and withdrawal of the rejections are respectfully requested.

The amendment to claims 1-4 and 110 (and further wherein the biostructure is obtainable by gravure coating, piezo-electric printing, or acoustic printing) are supported by the specification at, for instance, page 15, lines 6-7.

The amendment to claim 110 (three-dimensional) is supported by original claims 25 and 26.

Interview Summary

Applicant's Representative, Ann Mueting, thanks Examiners Cheu and Le for the interview granted on December 8, 2004. It is noted that the Examiner indicated that Thiagarajan et al. is not a proper 35 U.S.C. §102 reference. It is further noted that, although the Examiner indicated it would not be necessary to amend the claims (e.g., in a product-by-process format), several of the claims have been amended in an attempt to further prosecution.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 1-24, 48, and 100-110 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is rendered moot. Each of the independent claims has been amended to clarify that biological material is imbedded within the biostructure.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 1-2, 6-13, 15-24, 48, 100, and 109-110 under 35 U.S.C. §102(b) as being anticipated by Thiagarajan et al. (*European Federation of Biotechnology*, 1995; pgs. 304-312). This rejection is respectfully traversed.

Thiagarajan et al. teach a thin film plug reactor (TFPR) that can be used to study the physiology of *E. coli* that are permanently immobilized in thin films made from a latex copolymer of acrylic and vinyl acetate (pages 304 and 306). The TFPR consists of a glass chamber that contains an aluminum plug whose surface is coated with a mixture of copolymer and *E. coli* cell paste using a drawdown method (page 305). An alternative method uses cell + polymer-coated pressure sensitive polyester attached to the aluminum plug (page 305).

The Examiner states that Thiagarajan et al. teach a polyester as a nonporous latex (page 7 of the Office Action). However, polyester is not necessarily latex-derived, and there is no disclosure in Thiagarajan et al. that it is. Furthermore, in the previous Office Action the Examiner pointed to the aluminum plugs as being nonporous, and now in this Office Action the Examiner is apparently pointing to a silicone rubber sealant as being a porous material. Although this may be true, it is not at all clear how this applies to Applicants' invention.

The plug reactor was described as being a model system for designing porous immobilization media and bacterial cells to sustain biocatalytic activity for long periods of time (page 312). The films used within a TFPR are described as exhibiting diffusion properties that are related to polymer particle coalescence and film structure, which further indicates the porous nature of the films, as diffusion would not occur through a nonporous film. Thiagarajan et al. used the TFPR to study oxygen uptake from medium that was in contact with the film of the TRPR.

Claims 1, 2, 11, 12, 18, 22, 109 and 110 are directed to a composite biological device comprising a biostructure comprising at least one biological material .... wherein at least a portion of the biostructure comprises a nonporous latex-derived material.

Claims 48, 100-105 and 107-108 are directed to a method of determining the presence of an analyte in a sample ..... upon contact with the analyte, the biological material produces a response and emits a signal; and detecting the signal. Furthermore, the methods include use of a device that comprises a nonporous latex-derived material.

Thiagarajan et al. do not teach a device that includes a nonporous latex-derived material (claims 1, 2, 11, 12, 18, 22, 109 and 110). In addition, Thiagarajan et al. do not teach a method

to determine the presence of an analyte, or a method wherein a biological material produces a response and emits a signal upon contact with an analyte (claims 48, 100-105 and 107-108). Therefore, Applicants respectfully submit that Thiagarajan et al. do not anticipate the claims and reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 102(b) are respectfully requested.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 3 and 101 under 35 U.S.C. §103(a) as being unpatentable over Thiagarajan et al. in view of Inouye et al. (EP 0 314 338). This rejection is rendered moot in view of the amendment to claim 3. Although Applicants do not agree with the Examiner, this has been done in an effort to expedite prosecution.

The Examiner rejected claims 103-108 under 35 U.S.C. §103(a) as being unpatentable over Thiagarajan et al. in view of Mulchandani et al. (*Analytic Chem.*, 1998; *70*:4140). This rejection is traversed for the reasons discussed above. Mulchandani et al. do not rectify the deficiencies of Thiagarajan et al.

The Examiner rejected claims 1-20, 22, 48, and 109-110 under 35 U.S.C. §103(a) as being unpatentable over Cantwell et al. (EP 0 288 203) in view of Inouye et al.

Cantwell et al. teach immobilized cells in which bacterial or fungal cells are immobilized in intimate admixture with a solid organic polymer, and to processes for the preparation and use thereof (page 2, lines 3-5). The structure and permeability to aqueous media of the compositions "is such that a substrate is allowed access to the cells containing the enzyme to which it is to be subjected; a composition allowing suitable water permeability is used, e.g. acrylates are often preferred to polyvinylidene chloride (which tends to be a barrier to H_2O)" (page 4, lines 47-50). Cantwell et al. further emphasize the preparation of porous compositions that allow a substrate to come into contact with a cell and thereby teaches away from composite devices that include

nonporous components (although porous components can also be a part of Applicants' claimed composite device).

Applicants' claims recite a composite biological device comprising a biostructure comprising at least one biological material ..... wherein at least a portion of the biostructure comprises a nonporous latex-derived material ..... wherein the biological material is metabolically active or becomes metabolically active.

Inouye et al. teach a microplate. This is not a composite device that has biological material imbedded with a biostructure. Thus, there is no obvious connection between Inouye et al. and Cantwell et al. Accordingly, it is respectfully requested that this rejection be withdrawn.

With respect to claims 1-4 and 110 as amended, it was surprisingly found by Applicants that using printing methods selected from gravure coating, piezo-electric printing, and acoustic printing, can provide biostructures wherein the biomaterial, which is an integral part thereof, remains viable over extended periods of time and shows activity when used in assays. It was not recognized, prior to Applicants' invention, that such results could be achieved using these printing methods.

The cell-containing latex biosensor patch described in the paragraph from line 24 on page 29 to line 6 on page 30 of the present description is, for example, prepared by piezo-electric printing, has a patch thickness of 3 μm after four coatings, and shows high activity in the detection of mercury.

For certain embodiments (e.g., claim 110), the devices include three-dimensional (3-D) biostructures. Such 3-D microstructures have additional advantages. For example, they have the potential to allow molecules to be screened to pass through multiple environments or reaction zones before reaching the target biomaterial incorporated in the biostructure. This can be useful in applications where certain chemical transformations of an analyte are necessary before it can be detected.

Furthermore, the printing methods of the present claims, especially piezo-electric or acoustic printing methods, when compared to rod, bar, or slot coating methods, can immobilize

biomaterial in high resolution multilayer microstructures, which can be in the form of a patch, of such high density (e.g., number per unit area) and high specific activity (e.g., number of cells per microstructure) that remarkable gains can be realized in biosensor sensitivity, biocatalyst volumetric activity, screening sensitivity, and productivity (e.g., the paragraph from line 27 on page 15 to line 23 on page 16 of the present application).

By these methods, biological material can be ejected or jetted in pico-liter size droplets. A matrix material, e.g., polymeric material, can be combined with the biological material or applied separately by using fusing streams, and millions of single droplets can be deposited in ultra-high densities (e.g., greater than about 1000 dots per inch) at very high rates. Such methods allow, for instance, the use of ink-jet heads which contain several rows of nozzles, each nozzle acting as a separate pump and each row feeding from a separate reservoir, mixing of at least 4 different liquid streams as they are deposited resulting in the creation of one or multiple gradients during deposition. In addition, individual rows of nozzles can be washed and refilled any number of times with new media by a multi-channel wash and refill position during the printing operation.

Thus, a biostructure can be built up in the form of an assembly comprising a large number of three-dimensional micro-wells, if desired, comparable to an extremely small microtiter plate. Thus, on a small area of an assembly patch a large number of reaction zones can be created, each with it own microenvironment (e.g., the micro-wells can contain distinct microorganisms), so that a large number of assays can be effected simultaneously in a short time, using only small amounts of device material. For example, an assembly containing hundreds or thousands of distinct wells would allow the screening of compounds by applying the assembly patch onto a test organism.

Summary

It is respectfully submitted that the pending claims 1-4, 11, 12, 14, 16, 18, 22, 109, and 110 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 15th day of December, 2004, at 6:55 pm (Central Time).

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